Methods: Patients with peripheral tumors ≤ 5 cm are treated with SBRT without body frame to 54 Gy in 3 fractions within 8-10 days. For treatment planning, a 4DCT reference scan is acquired representing the patients anatomy over the breathing cycle. From this 4D dataset, a single 3D frame is extracted with the tumor and surrounding anatomy in their time averaged mean position. The Planning-Target-Volume (PTV)-margins depend on the patient specific tumor amplitude. Organs-at-risk (OAR) are delineated and automatically expanded by 1 cm to validate that corrections up to 1 cm during treatment delivery can be safely executed without violating fixed dose constraints. Before each treatment fraction, the linac integrated CBCT scanner is used to acquire a new 4D data set (Figure 1a). A local rigid registration technique is used to measure the tumor trajectory after which the time averaged tumor misalignment is calculated and corrected with a couch shift. At the end of the treatment fraction another 4D-CBCT scan is acquired to determine intrafraction stability.

Results: So far 34 patients have been treated with SBRT in our institution. Residual treatment delivery inaccuracies were analyzed for the first 20 patients. Based on these results, the required PTV-margin were calculated to account for delineation uncertainties (2 mm SD in each direction), breathing motion, residual setup errors and intrafraction baseline variation (both ≤ 2 mm (1 SD) systematic and random) as shown in Figure 1b. For example at a 1 cm tumor amplitude, a total margin of only 0.7 cm is required. Compared to a bony anatomy driven correction protocol combined with an Internal-Target-Volume (ITV) approach to account for respiratory motion this is a 49% reduction. For all patients, tumor-to-bony anatomy discrepancies never exceeded 1 cm and post treatment validation scans did not show unacceptable deviations.

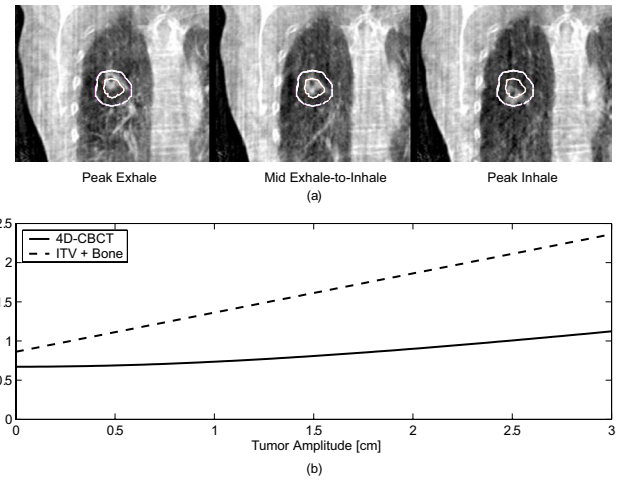

Figure 1: a) Coronal slices of three frames of a 4D-CBCT scan acquired just prior to SBRT treatment. Despite some artifacts, tumor motion and accurate alignment can be easily verified. b) Cranial-caudal GTV-to-PTV margin (no CTV margin used) required to account for delineation uncertainties, breathing motion, residual setup error and intrafraction variability as a function of tumor peak-to-peak amplitude: using 4D-CBCT guidance compared to a bony anatomy driven protocol combined with an ITV approach. Even at large tumor amplitudes margins are relatively small due to accurate guidance, shallow penumbra in lung and dose prescription to relative low iso-doses (typically 70% to 80%).

Conclusion: SBRT without body frame can be safely administered using 4D-CBCT guidance. Even with considerable breathing motion the PTV-margins can safely be kept relatively small allowing patients with larger tumor volumes to benefit from the advantages of SBRT.

B5-06 **NSCLC: New Paradigm in Radiation Therapy, Tue, 13:45 - 15:30**

Mature results of PulmonArt: Involved-field 3D radiotherapy (RT) and docetaxel/cisplatin chemotherapy (CT) in a randomised phase 2 study comparing concurrent CT-RT followed by consolidation CT, with induction CT followed by concurrent CT-RT in patients (pts) with stage III non-small cell lung cancer (NSCLC)

Van Meerbeeck, Jan P.[1] Cardenal, Felipe[2] Vansteenkiste, Johan[3] Stigt, Jos[4] Akyol, Fadil[5] De Neve, Wilfried[6] Bakker, Joke[7] Dupont, Jean Michel[8] Scagliotti, Giorgio V.[9] Senan, Suresh[10]

[1] University Hospital, Ghent, Belgium [2] Institut Catala d'Oncologia, Medical Oncology, Barcelona, Spain [3] University Hospital Gasthuisberg, Respiratory Diseases, Leuven, Belgium [4] Isala Ziekenhuis, Pulmonology, Zwolle, The Netherlands [5] Hacettepe University, Radiation Oncology, Ankara, Turkey [6] University Hospital, Radiation Oncology, Ghent, Belgium [7] sanofi-aventis, Medical Affairs and Clinical Operations, Gouda, The Netherlands [8] PRA-International, Paris, France [9] San Luigi Hospital, Thoracic Oncology, Torino, Italy [10] VU Medical Center, Radiation Oncology, Amsterdam, The Netherlands

Background: Platinum-based CT-RT improves survival in stage III NSCLC compared to RT, although with increased toxicity. Drug doses in most concurrent schemes are suboptimal for systemic activity, and full dose induction or consolidation CT appears advantageous. Some trials had suggested that induction CT followed by concurrent RT was not superior to concurrent RT followed by consolidation CT. Docetaxel (D) is active in NSCLC, has radiosensitising effect and is promising when given as consolidation agent.

Aim: Randomised phase 2 trial comparing the toxicity/safety and efficacy of CT followed by CT-RT (IND) vs. CT-RT followed by CT (CON).

Methods: Eligible pts had unresectable stage III NSCLC and WHO PS 0-1, weight loss ≤10%, adequate renal, pulmonary, haematological and hepatic function. Induction and consolidation CT consisted of D 75 mg/m^2 on d1 and cisplatin (C) 40 mg/m^2 on d1&2, both q3 wks for 2 cycles. CT-RT consisted of D 20 mg/m^2 and C 20 mg/m^2 both given on d1 weekly for 6 wks, concurrent with 66 Gy (2 Gy/d, 5 d/w for 6.5 wks). Toxicity was reduced using the following approaches: 1. Involved fields using 3D treatment planning; 2: exclusion of pts with V20 values >35 Gy from immediate concurrent CT-RT by cross-over to IND and treatment to a post-CT tumor volume. Toxicity/response was evaluated according to NCI-CTC/RECIST. With a type 1 error of 0.2, a power of 0.8 and allowing for 15% cross-over or ineligibility, a 70-pts sample size is needed to confidently exclude a grade 3-4 oesophageal toxicity rate of >25% in either arm. Toxicity and response were based upon actual treatment received; outcome is estimated in the ITT population.

Results: 70 patients with the following characteristics were enrolled: IND: 36/CON: 34; male (%): IND 75/CON 91; median age 61 y; squamous ca (%): IND 31; CON: 50; IIIB(%): IND 44/CON 68; PTV (cc): IND 288/CON 283. 5 pts switched from CON to IND. Treatment, response and toxicity data according to actual treatment received are in the table. ITT 1-year overall and progression free survival (PFS) rates (± 95% CI) are 56% ± 16% and 36% ± 16% for IND and 65% ± 17% and 53% ± 17% for CON (p =0.8 and 0.3)

Conclusions: Both IND and CON approaches have similar treatment intensity and duration, similar esophageal toxicity rates and comparable response rates. CON results in a trend towards a better PFS at the cost of a higher haematological toxicity.

Table (according to actual treatment received)	IND (N= 41)	CON (N= 29)	p
Median RDI docetaxel (%)	99	93	NS
Median RDI cisplatin (%)	99	96	NS
Median RDI radiotherapy (%)	100	100	NS
Overall treatment time (days)	87	72	NS
Grade 3/4 neutropenia / febrile neutropenia (%)	22/5	41/17	0.08/0.09
Gr 3/4 esophagitis/pneumonitis (%)	34/10	28/10	0.56/0.96
Gr 3/4 nausea/vomiting (%)	5	14	0.18
Deaths during and within 30 d of treatment	0	2	0.09
Best response at end of treatment (%)	68	83	0.17

B5-07 **NSCLC: New Paradigm in Radiation Therapy, Tue, 13:45 - 15:30**

The effect of NQO1 polymorphisms on prognosis of non-small cell lung cancer after postoperative radiation therapy

Song, Si Yeol[1] Choi, Eun Kyung[1] Lee, Jung Shin[2] Park, Heon Joo[3] Lee, Sang-Wook[1] Park, Seung Il[4] Kim, Dong-Kwan[4] Kim, Sang-We[2] Lee, Dae Ho[2] Lee, Yu Sun[1]

[1] Dept. of Radiation Oncology, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Korea [2] Dept. of Medical Oncology, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Korea [3] Dept. of Microbiology, College of Medicine, Inha University, Incheon, Korea [4] Dept. of Thoracic Surgery, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Korea

Purpose: NQO1 is an enzyme that catalyzes the two-electron reduction of the more toxic quinone to less toxic hydroquinone. It is known that NQO1 may decrease the risk of cancer development in normal human tissue, and NQO1 polymorphism affect on the treatment outcome after chemotherapy in lung cancer. We investigated the effect of NQO1 polymorphism on radiation therapy through the difference of survival outcome by NQO1 different genotypes in non-small cell lung cancer (NSCLC) patients treated with surgery followed by postoperative radiation therapy.

Methods: One hundred and fifty-two patients (Male: 116, Female: 36) who were histologically proven NSCLC and treated with surgery and postoperative radiation therapy from Jan 2000 to Aug 2005 were analyzed. We determined NQO1 genotypes from peripheral blood of patients. NQO1 genotypes were classified as three groups, and each genotype had different enzymatic activities; C/C is the wild type with normal activity, C/T is the heterozygous type with decreased activity, and T/T is the homozygous mutation with no enzymatic activity. Thereafter, we analyzed the correlation between NQO1 genotypes and the survival outcome after surgery and postoperative radiation therapy. For the authenticity of genotype from peripheral blood, genotypic analysis directly from tumor tissue was performed.

Results: Numbers of patients in each NQO1 genotype were 41 patients for C/C, 83 patients for C/T, and 28 patients for T/T. Patients characteristics with sex, age, clinical stage, pathology, and combined chemotherapy were not different between genotypic groups. Median follow-up period was 19.7 months. NQO1 genotype had an effect on the actuarial loco-regional control and survival. Patients expressing C/C and C/T genotype with NQO1 enzymatic activity had a significantly longer loco-regional progression free survival (89.2% vs. 68.3% at 2yr) and overall survival (90.2% vs. 70.6% at 2yr) than patients expressing T/T genotype (p=0.034). Genotypic analysis from tumor tissue was performed in only eighteen patients. There was accordance in sixteen patients between the genotype from peripheral blood and that directly from tumor tissue, and the other two patients with C/C genotype in blood expressed C/T in tumor tissue.

Conclusions: NQO1 polymorphisms affected on treatment results in NSCLC patients treated with surgery and postoperative radiation therapy. NQO1 could be a useful prognostic factor for NSCCL after radiation therapy, although the further study with more patients and long-term follow-up should be promised.

Session B6: Health Services, Supportive Care & QOL

Tuesday, September 4

B6-01 **Health Services, Supportive Care & QOL, Tue, 13:45 - 15:30**

Developing clinical guidelines on lung cancer for limited resource settings: an international collaboration supported by the International Atomic Energy Agency (IAEA)

MacBeth, Fergus[1] Cho, Kwan[2] Abratt, Raymond[3] Stephens, Richard[4] Jeremic, Branislav[5]

[1] Velindre Cancer Centre, CARDIFF, UK [2] National Cancer Centre, Goyang, Korea [3] Groote Schurr Hospital, Cape Town, South Africa [4] MRC Cancer Trials Unit, London, UK [5] International Atomic Energy Agency, Vienna, Austria

Introduction: Lung cancer is an increasing problem in developing countries, where access to medical resources may be limited. It is crucial that care in these settings makes most effective and cost effective use of those resources, based on good evidence. Clinical guideline recommendations from developed countries are not likely to be always (or ever) appropriate and so a different approach is needed.

Methods: An international panel, with a special interest in lung cancer, was invited to a meeting organised by the IAEA in March 2006, at which the main approaches were drafted. Reference was made to recent English language evidence-based clinical guidelines and to other recent systematic reviews, meta-analyses and research. Drafts were then circulated sequentially around the group members, a telephone conference held and a final version approved. We assumed that baseline resources for diagnosis (including CT scanning), radical surgery, radiotherapy (RT) with at least 60Co and 2D planning and IV cisplatin-based combination chemotherapy (CT) would be available. Tables were constructed that showed a baseline standard treatment for different patient groups and the additional benefits, risks and resource use from additional treatment options. Accompanying text summarised the evidence and justification for these options.

Results: Six tables were devised entitled:

1. Options for patients with limited disease SCLC and good prognosis
2. Options for patients with operable NSCLC
3. RT options for patients with medically inoperable NSCLC (Stage I and II)
4. Options for patients with inoperable 'small' volume NSCLC ('Favourable' Stage III)
5. Options for palliative thoracic RT